

**REMARKS**

Claims 1-22 and 28-32 are pending. Claims 17-22 are withdrawn from consideration. By virtue of this response, claims 2-5, 7-16, 18, 19, and 28-32 have been amended to substitute “the” for “a” to reflect their status as dependent claims. No new matter is added. Accordingly, claims 1-16 and 28-32 are currently under examination.

Regarding the Examiner’s statement in section 1 of the Office Action issued on 07/28/2009, Applicant wishes to clarify that claim 3 recites a peptide comprising the amino acid sequence GPRLGYSWHE (SEQ ID NO:1), which is the retro-inverso form of the naturally occurring GnRH.

***35 USC § 112, Second Paragraph*****Rejection under 35 U.S.C. § 112, second paragraph**

Claim 1-16 and 28-32 are rejected under 35 U.S.C. § 112, *second paragraph*, as allegedly being indefinite. Applicant respectfully traverses.

The Examiner stated that the recitation of “D-amino acids” in claims 1 and 3-5 is unclear as to whether it refers to retro-inverso amino acids of the amino acid sequences or D isomer configuration of the amino acid sequences. Office Action at page 3. Applicant respectfully disagree with the Examiner’s statement that the recitation of “D-amino acids” is indefinite.

Applicant submits that one of ordinary skill in the art would readily understand that the phrase “wherein the amino acids are D-amino acids” in the claims means that the amino acids in the sequence are D-amino acids, not L-amino acids.

The present application provides a retro-inverso (RI) gonadotropin-releasing hormone (GnRH) peptide. The specification provides:

The invention describes a retro-inverso gonadotropin-releasing hormone (GnRH) peptide which is capable of eliciting an immune response directed against GnRH, the peptide having the amino acid sequence GPRLGYSWHX, wherein the amino acids are D-amino acids and X is any amino acid.

Paragraphs [0043].

Retro-inverso (RI) peptides are peptides where the amino acid residues are aligned in the reverse order of that in the parent peptide and D-amino acids replace the L-amino acids of the parent peptide, making the RI-peptides powerful immunogens. The orientation of the side chains in a RI-analog is very similar to that in the parent peptide, which leads to eliciting antibodies that cross-react strongly with the parent L-structure.

Paragraphs [0046].

Therefore, in view of the specification, one of ordinary skill in the art would readily understand that the recitation of “D-amino acids” means that the amino acids in the recited sequence are D-amino acids in the claims.

In view of the foregoing, Applicant respectfully request that the rejection of claims 1-16 and 28-32 under 35 U.S.C. § 112, *second paragraph*, be withdrawn.

**Claim Objection**

Claims 2-5, 7-16, and 28-32 are objected to because they are dependent claims but recite “a peptide” and “a vaccine” in the preamble.

Applicant has amended the claims to substitute “the” for “a.” Therefore, the claim amendment renders the objection moot.

In view of the foregoing, Applicant respectfully requests that the objection of claims 2-5, 7-16, and 28-32 be withdrawn.

**Rejections Under 35 USC § 102**

**Rejection under 35 U.S.C. § 102(b) over Mathias**

Claims 1-3 and 30 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Mathias (U.S. Pat. No. 5,434,136). Applicant respectfully traverses.

The Examiner stated that Mathias discloses a peptide with the sequence shown as GPRLGYSWHE (SEQ ID NO:1) in the Sequence Listing section of the patent, which is identical to the SEQ ID NO:1 of the presently claimed invention and thus anticipates claims 1-3 and 30. *See* Office Action at page 3. Applicant respectfully disagrees.

To serve as an anticipating reference, the disclosure must be enabled. *Elan Pharm., Inc. v. Mayo Found. Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1375 (Fed. Cir. 2003). Enablement requires that the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. *Id.* The disclosure must be such as will give possession of the invention to the person of ordinary skill. *Id.* at 1055. “Even the act of publication or the fiction of constructive reduction to practice will not suffice if the disclosure does not meet this standard.” *Id.*

The present invention provides a retro-inverso gonadotropin-releasing hormone (“GnRH”). The specification provides:

The invention describes a retro-inverso gonadotropin-releasing hormone (GnRH) peptide which is capable of eliciting an immune response directed against GnRH, the peptide having the amino acid sequence GPRLGYSWHX, wherein the amino acids are D-amino acids and X is any amino acid. More particularly, X is E, Q, P or G, and even more particularly, X is E or Q. Thus, a preferred amino acid sequence for the peptide is GPRLGYSWHE (SEQ ID NO:1).

Paragraph [0043].

Retro-inverso (RI) peptides are peptides where the amino acid residues are aligned in the reverse order of that in the parent peptide and D-amino acids replace the L-amino acids of the parent peptide, making the RI-peptides powerful immunogens. The orientation of the side chains in a RI-analog is very similar to that in the parent peptide, which leads to eliciting antibodies that cross-react strongly with the parent L-structure.

Paragraph [0046].

Applicant submits that Mathias does not anticipate claims 1-3 and 30 since the allegedly anticipatory sequence, namely, GPRLGYSWHE (SEQ ID NO:1) (as appeared in the Sequence Listing section of the patent), has never been contemplated and the allegedly disclosure of the sequence is not enabled for 35 U.S. C. § 102 purposes.

Mathias teaches a method of treating disease with GnRH analogs. *See* column 2, lines 44-47. According to Mathias, the preferred analogs of GnRH are similar to GnRH but with particular D-amino acid substitutions. *See* column 2, lines 52-55. Mathias states that the synthesized analogs of GnRH have a D-amino acid substitution at position 6. *See* column 3, lines 52-56. Additional GnRH analogs contemplated by Mathias are analogs of substituted natural and synthetic amino

acids in either the D or L configuration, peptides of greater than or less than 10 amino acids, peptides with varied sugar linkages and additional modifications which do not destroy the agonistic or antagonistic properties of the GnRH analog. *See* column 4, lines 40-47. Therefore, Mathias does not teach or contemplate the retro-inverso GnRH where the amino acid residues are aligned in the reverse order of that in the parent peptide and the amino acids are D-amino acids.

The allegedly anticipatory sequence concerns the sequence of SEQ ID NO:1 in Mathias. Column 3, lines 46-49 in the Detailed Description section of Mathias provides a description and the sequence for SEQ ID NO:1:

Naturally occurring GnRH has the following amino acid sequence:  
pGlu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH<sub>2</sub>  
(*Seq. Id. No. 1*)

(emphasis added).

However, SEQ ID NO: 1 in the Sequence Listing section of Mathias shows the sequence of “Gly-Pro-Arg-Leu-Gly-Tyr-Ser-Trp-His-Glu,” which is the sequence stated in the Detailed Description section (*see above*) in the reverse order (*i.e.*, amino acid resides aligned in the reverse order). Thus, the sequence for SEQ ID NO:1 shown in the Sequence Listing section is an error. The correct sequence for SEQ ID NO:1, the naturally occurring GnRH, is Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly, as shown in the Detailed Description section at column 3, lines 46-49.

Therefore, one of ordinary skill in the art, in reading Mathias as a whole, would readily conclude that the sequence of SEQ ID NO: 1 in the Sequence Listing section of Mathias, namely, Gly-Pro-Arg-Leu-Gly-Tyr-Ser-Trp-His-Glu, is a typographical error and the correct sequence for SEQ ID NO: 1 is Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly, as stated in the Detailed Description section at column 3, lines 46-49. Accordingly, one of ordinary skill in the art would readily conclude that Mathias does not teach or contemplate the allegedly anticipatory sequence, namely, Gly-Pro-Arg-Leu-Gly-Tyr-Ser-Trp-His-Glu.

The disclosure of the allegedly anticipatory sequence in Mathias is a disclosure by typographical error and is not an enabling disclosure. The disclosure of this nature does not teach one of ordinary skill in the art how to make or use the allegedly anticipatory sequence. In addition, it does not give possession of the allegedly anticipatory sequence to one of ordinary skill in the art. The disclosure taken as a whole relates to and envisions only the naturally occurring sequence of

GnRH with particular D-amino acid substitutions and not the reverse order of the naturally occurring GnRH sequence. The disclosure of the reverse order of the naturally occurring GnRH in the Sequence Listing section is an obvious error. Therefore, Mathias is not an enabling reference for 35 U.S.C. § 102 purposes and thus does not anticipate the present claim 1. In addition, Mathias does not anticipate claims 2, 3, and 30, which depend from claim 1.

In view of the foregoing, Applicant respectfully requests that the rejection of claims 1-3 and 30 under 35 U.S.C. § 102(b) over Mathias be withdrawn.

Rejection under 35 U.S.C. §102(b) over Meloen

Claims 1-16 and 28-32 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Meloen (U.S. Pat. No. 7,361,349). Applicant respectfully traverses.

Meloen allegedly discloses the sequence “pGlu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH<sub>2</sub>.” *See* column 1, line 54. The Examiner stated that such sequence reads on claims 1-3. Office Action at page 4. Applicant respectfully disagrees.

Applicant submits that Meloen does not teach the sequence recited in claim 1 or other dependent claims. The specification of Meloen, at column 1, line 54, states that the amino acid sequence of GnRH-1 can be represented as pGlu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH<sub>2</sub>. As discussed above, such sequence is a naturally occurring sequence of GnRH, which is not what is claimed in the present claims.

The present application provides a retro-inverso GnRH, wherein the amino acid residues are aligned in the reverse order of that in the parent peptide and D-amino acid replace L-amino acids of the parent peptide. *See* the specification at paragraphs [0043] and [0046]. The sequence disclosed in Meloen, namely, Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly, is the reverse order of the sequence recited in claim 1, namely, Gly-Pro-Arg-Leu-Gly-Tyr-Ser-Trp-His-X. Therefore, Meloen does not anticipate claim 1. In addition, Meloen does not anticipate claims 2-16 and 28-32 which depend from claim 1.

In view of the foregoing, Applicant respectfully requests that the rejection of claims 1-16 and 28-30 under 35 U.S.C. § 102(e) over Meloen be withdrawn.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 638772009900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 28, 2010

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